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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,211	09/03/2002	Barry Teobald	ASZD-P01-210	9302

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,211	TEOBALD, BARRY	
	Examiner	Art Unit	
	Deepak R Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *10,11 and 13-19* is/are rejected.

7)☐ Claim(s) *1-9,12 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *02262002*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-21 are pending in this application.

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-20, drawn to compounds formula (I), corresponding composition, method of use and process of preparation.

Group II, claim(s) 21, drawn to compounds of formula (II).

Group III, claim(s) 21, drawn to compounds of formula (III) or (V).

Group IV, claim(s) 21, drawn to compounds of formula (IV).

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The compounds of Groups I-IV are drawn to structurally dissimilar compounds. They are made independently and used independently. They would be expected to raise different issues of patentability if a compound of Group I were anticipated, the anticipatory reference would not necessarily render obvious the other groups II-IV or vice-versa. They are not art recognized equivalents and require separate searches in the literature. Inventions II-IV and I are related as mutually exclusive species in an intermediate-final product relationship. Distinctness is proven for claims in this relationship if the intermediate product is useful to make other than

the final product (MPEP § 806.04(b), 3rd paragraph), and the species are patentably distinct (MPEP § 806.04(h)). In the instant case, the intermediate product is deemed to be useful to make other compounds distinct from the instantly claimed compounds and therefore, the inventions are deemed patentably distinct since there is nothing on this record to show them to be obvious variants. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention. Further, under PCT Rule 13.2, unity of invention is considered to be present if the intermediate and the final product have the **same structural element**, see MPEP Appendix AI, Annex B, Part 1 (g), which is not found in the instant case.

During a telephone conversation with Mr. David Halstead on December 12, 2003 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-20. Affirmation of this election must be made by applicant in replying to this Office action. Claim 21 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: TRIAZOLO[4,5-d]PYRIMIDINYL COMPOUNDS.

Claim Objections

Claims 1-20 are objected to because of the following informalities:

(a) Claim 1 does not end with a period.

(b) In claim 8, there are multiple periods, see page 25, lines 20-21.

Appropriate correction is required.

Claim 3 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can not refer to two different claims to different features. See MPEP § 608.01(n).

Claims 4-7 and 9-19 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can not depend from any other multiple dependent claim. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-11 and 13-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of the diseases, does not reasonably provide enablement for **prevention** of the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims recite 'treatment or **prevention'** of diseases related to platelet aggregation inhibitors, which diseases are identified as myocardial infarction, thrombotic stroke, etc. The scope of the claims includes not only treatment but also "**prevention** of a disease" which is not adequately enabled solely based on the activity of the compounds provided in the specification at pages 21-22. The instant compounds are disclosed have thrombin inhibitory activity and it is recited that the instant compounds are useful in 'treatment or prevention' of several diseases, including thrombotic stroke, unstable or stable angina, etc., for which applicants provide no competent evidence. "To prevent" actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed 'preventive' effect solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Clemetson, (PubMed Abstract enclosed) wherein with regards to platelet inhibitors, it is stated that "Since platelet inhibitors for long-term prophylaxis of cardiovascular diseases are in clinical trials there are many unanswered questions about long-term effects both positive and negative". Also, Cavallini et al., (PubMed Abstract enclosed)

with regards to therapeutic approach of myocardial disorders, conclude that 'Numerous other questions remain unanswered'. Goldschmidt-Clermont et al., in their recent article stated that 'Despite spectacular progress in the cardiovascular discipline, several key questions remain unanswered'. (Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Use of the compounds in **prevention** of diseases that require $P_{2\tau}$ receptor antagonistic activity.

2) The state of the prior art: Many recent publications have expressed that there are many issues to be resolved, concluding that the activity of the inhibitors is unpredictable.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for the 'preventive' effect of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: The specification does not provide any dosage regimen for the claimed preventive benefit, which dosage requirements generally depend on a variety of factors.

6) The breadth of the claims: The instant claims embrace not only treatment but also the **prevention** of diseases.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards 'prevention' of the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Duplicate Claims

Applicant is advised that should claim 1 be found allowable, claim 12 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a

substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 12 recites the intended use of the compound and does not further limit claim 1.

Applicant is advised that should claim 9 be found allowable, claims 10-11 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 10 and 11 recite the intended use of the composition and do not further limit claim 9.

Allowable Subject Matter

Claims 1-9 and 20 would be allowable if the claim objections are overcome. The closest reference of record, WO 99/05143does not teach pyrrolidine group attached to the triazolo[4,5-d]pyrimidine group.

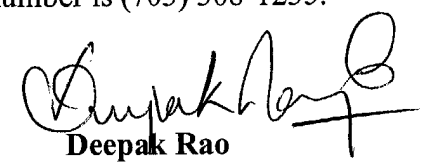
Receipt is acknowledged of the Information Disclosure Statement filed on February 26, 2002 and a copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (703) 305-1879. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (703) 308-4716. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.



Deepak Rao
Primary Examiner
Art Unit 1624

12/12/03